

Short report

Olfactory threshold in Parkinson's disease

N P QUINN, M N ROSSOR, C D MARSDEN

From the University Department of Neurology and Parkinson's Disease Society Research Centre, Institute of Psychiatry and King's College School of Medicine, London, UK

SUMMARY Olfactory threshold to differing concentrations of amyl acetate was determined in 78 subjects with idiopathic Parkinson's disease and 40 age-matched controls. Impaired olfactory threshold (previously reported by others) was confirmed in Parkinsonian subjects compared with controls. There was no significant correlation between olfactory threshold and age, sex, duration of disease, or current therapy with levodopa or anticholinergic drugs. In a sub-group of 14 levodopa-treated patients with severe "on-off" fluctuations, no change in olfactory threshold between the two states was demonstrable. Olfactory impairment in Parkinson's disease may involve mechanisms that are not influenced by pharmacologic manipulation of dopaminergic or cholinergic status.

Impaired olfactory threshold^{1 2} and discrimination² have previously been reported in patients with Parkinson's disease. Ward *et al.*,² found no correlation between degree of olfactory impairment and age, duration of disease, disease severity, and presence or nature of anti-Parkinsonian treatment. Because olfactory deficit constitutes one of a small number of non-motor deficits recorded in Parkinson's disease, we too have compared olfactory threshold in 78 subjects with a clinical diagnosis of idiopathic Parkinson's disease and 40 age-matched control subjects. Among the Parkinsonian subjects, 14 patients with severe "on-off" fluctuations were tested in both the "on" and "off" conditions.

Patients and methods

Seventy eight patients (50 male, 28 (36%) female), aged 36–85 (mean 61.5) years, with a clinical diagnosis of idiopathic Parkinson's disease were tested. Subjects with suspected dementia, or history of significant head injury or nasal disease were excluded. Sixty four subjects were currently receiving treatment with levodopa preparations (with or without additional anti-Parkinsonian medication), whilst 14 had never been treated with levodopa. Twenty eight were receiving anti-cholinergic drugs whilst 50 were not. Olfactory thresholds in patients were compared with the results from a group of 40 age-matched control subjects (27 male, 13 (32.5%) female).

Ten different dilutions of amyl acetate in liquid paraffin

Address for reprint requests: Dr NP Quinn, Kings College Hospital, London SE5 9RS, UK.

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were made up. The concentrations (in volumes %) were 0.005, 0.01, 0.025, 0.05, 0.1, 0.25, 0.5, 1.0, 2.0 and 4.0. For each screw-top glass test-tube containing amyl acetate, three identical tubes containing liquid paraffin only were also prepared. At each dilution, beginning in the middle of the range to minimise fatigue, each subject sniffed each of four tubes (one active, three "dummy") presented by the examiner in turn, and then gave the number of the tube thought to contain the smell. The threshold was taken as the highest dilution at which at least two out of three consecutive presentations were correctly identified. A numerical score for olfactory threshold was allotted as follows: 10 points for correctly identifying the most dilute tube down to 1 point for the most concentrated, with a score of 0 for failing to identify correctly even the most concentrated tube.

Results

Mean olfactory score (table) for the entire group of 78 patients (4.9 ± 2.9), was significantly lower than for the 40 normal control subjects (7.0 ± 2.4); $p < 0.001$, Mann-Whitney U test.

Fourteen Parkinsonian patients who were experiencing severe "on-off" fluctuations were tested both in the "on" and in the "off" condition. Five performed better "on" than "off", five worse, and in four there was no difference. Mean olfactory score when "on" was $5.1 (\pm 2.6)$, and when "off" $5.4 (\pm 2.4)$ (difference not significant).

Sixty-four patients were currently treated with either a levodopa-based preparation or a direct dopamine agonist, or both, whilst 14 had never been treated with dopaminergic drugs. Olfactory score in the former was 4.9 ± 3.0 , and in the latter 5.2 ± 2.6

Table

	n	Mean age (yr)	Mean disease duration (yr)	Mean olfactory threshold score	
Parkinson's disease	78	61.5 ± 10.3	9.8 ± 6.3	4.9 ± 2.9	} p < 0.001 Mann Whitney U test
Controls	40	62.5 ± 10.2	—	7.0 ± 2.4	
Levodopa treated	64	61.1 ± 10.3	11.2 ± 5.9	4.9 ± 3.0	} NS
No levodopa	14	63.6 ± 10.3	3.6 ± 3.6	5.2 ± 2.6	
Anticholinergics	28	59.8 ± 11.2	10.2 ± 7.2	4.9 ± 2.8	} NS
No anticholinergics	50	62.5 ± 9.7	9.3 ± 5.9	4.9 ± 3.0	
ON/OFF: ON	14	55.1 ± 9.4	13.6 ± 5.5	5.1 ± 2.6	} NS
OFF				5.4 ± 2.4	

(difference not significant). Twenty-eight patients were currently treated with anticholinergic drugs, whilst 50 were not currently receiving such preparations. Olfactory score in the former was 4.9 ± 3.0 , and in the latter 4.9 ± 2.8 . Overall, there was no significant correlation between olfactory score and age, sex, or duration of disease.

Discussion

This study confirms the previously reported impairment of olfactory threshold in Parkinson's disease patients.^{1,2} The absolute olfactory threshold to amyl acetate in our subjects differs considerably from that found by Ward *et al.*² However, this is probably explicable in terms of differing methodology: Ward *et al.*'s subjects were not allowed any false positive replies, whilst ours were allowed a maximum of one incorrect out of three consecutive responses. Another difference concerns the sex distribution of the population studied. It is known that there exists a difference between the sexes in odour identification, with females performing better than males.³ Because in the study of Ward *et al.* 66% of controls were female as opposed to 37.5% of patients, it might be argued that the poorer performance of the latter was wholly or partly due to the lower proportion of female subjects. In contrast, there was a slightly higher proportion of females in our patient group than in our controls, and yet the patient group still performed less well in the test than the control group.

What factors might be responsible for impaired olfaction in Parkinson's disease? Since the major neurochemical deficit in this illness is dopaminergic, and significant amounts of dopamine are normally present in the olfactory tubercle,⁴ impaired dopaminergic transmission would seem a prime suspect. In our patients, however, there was no significant difference in olfactory threshold either between levodopa-treated subjects and those who had not taken levodopa, or between the "on" and "off" states in subjects with severe motor fluctuations on levodopa treatment.

Reduced cortical choline acetyltransferase activity is a feature of Alzheimer's disease shared by many Parkinsonian subjects. Alzheimer's disease brains also show neurofibrillary tangles in anterior olfactory

nucleus,⁵ together with reduced choline acetyltransferase activity in olfactory tubercle.⁶ In addition, defective olfactory recognition has also been reported in subjects with both Alzheimer type dementia and Parkinsonian dementia.⁷ Therefore perhaps impaired olfactory threshold in patients with Parkinson's disease might be due to a cholinergic, rather than a dopaminergic, disturbance. However, in our material again no difference in olfactory threshold between Parkinsonian patients receiving and those not receiving anticholinergics could be detected. Thus, olfactory threshold in Parkinsonian subjects does not appear to be influenced by pharmacologic manipulations of dopaminergic and cholinergic transmission. Although this does not preclude a causative role for altered dopaminergic or cholinergic function, deficits in other monoaminergic or peptidergic transmitters, such as N-acetyl aspartylglutamate⁸ may underlie this so-far unexplained clinical finding.

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